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EXAMINER				
ZARA, JANE J				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/505,153

Applicant(s)

SUZUKI ET AL.

Examiner

Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 5, 7-10, 16, 18, 19, 21, 22, 27, 28, 30, 37 and 39-42 is/are pending in the application.
- 4a) Of the above claim(s) 16, 19, 21, 22, 27, 28, 30, 37, 39 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 5, 7-10, 18, 41 and 42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

This Office action is in response to the communication filed 2-8-08.

Claims 1, 4, 5, 7-10, 16, 18, 19, 21, 22, 27, 28, 30, 37, 39-42 are pending in the instant application.

Claims 16, 19, 21, 22, 27, 28, 30, 37, 39 and 40 have been withdrawn as being drawn to a non-elected invention. Claims 1, 4, 5, 7-10, 18, 41 and 42 have been examined on their merits as set forth below. The non-elected methods claims that are identical in scope with the elected claims will be rejoined and examined on their merits upon indication of allowance of the elected claims 1, 4, 5, 7-10, 18, 41 and 42.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The declaration under 37 CFR 1.132 or 1.131, filed 2-8-08 is insufficient to overcome the rejection of claims 1, 4, 5, 7-10, 18, 41 and 42 based upon written description as set forth in the last Office action for the reasons set forth below.

Response to Arguments and Amendments

Applicant's arguments with respect to claims 1, 4, 5, 7-10, 18, 41 and 42 under 35 U.S.C. 102(b) have been considered but are moot in view of the new ground(s) of rejection set forth below.

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections/Rejections Necessitated by Amendment

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5, line 5 recites the term "inward expression." It is unclear whether this refers to expression in subcellular or cellular orientation, or alternatively that the expression product is not secreted outside of the cell and therefore remains "inward." Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5, 7-10, 18, 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the Office action mailed 10-10-07.

The claims are drawn to recombinant vector encoding (I), (II), or (III), which vector encodes an RNAi molecule, or a partially self-complementary polynucleotide with RNA suppression activity in relation to RNA having a sequence complementary to either component (I) or (III) or a partial sequence thereof, and which vector also comprises the intervening (II), which optionally comprises a sequence having decoy activity, a

sequence having any of RNase suppression activity, antisense activity, ribozyme activity or transfer RNA, or any combinations thereof.

Applicant's arguments and declaration filed 2-8-08 have been fully considered but they are not persuasive. Applicant argues that the instant invention is sufficiently described and that the design of the single stranded polynucleotide comprising continuous components (I), (II) and (III) uses common techniques known in the art. Applicant also provides examples of successful gene inhibition in the Declaration filed 2-8-08 using siRNA targeted to luciferase.

Contrary to Applicant's assertions, the Declaration, specification and claims do not adequately describe or provide a representative number of species of the claimed genus to satisfy the written description requirements for the instantly claimed invention, nor has Applicant adequately described elements which appear to be essential to the claimed functions. The examples provided in the instant disclosure and Declaration comprise siRNA encoded by a recombinant vector, which comprise sequences with complete homology to the control target luciferase gene, and further comprising the adjoining loop region between self-complementary siRNA strands. The examples provided, however, do not provide adequate description, or show possession at the time of filing, of a representative number of species of the genus claimed, comprising partially self-complementary polynucleotides with RNA suppression activity to any target gene, whereby RNA suppression activity has been shown in relation to RNA having a sequence complementary to either component (I) or (III) or a partial sequence thereof.

Furthermore, the instant specification provides mere mention of possibly including within the intervening component (II) sequences including cytoplasm translocation sequences, sequences having decoy activity, interferon induction suppression sequences, or sequences having RNase suppression activity. But mere mention of the possibility of including these sequences, without the inclusion of these sequences within the actual constructs, and without any examples of providing the functions claimed in an expressed construct, do not substitute for actual possession at the time of filing.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of constructs claimed, including cytoplasm translocation sequences, decoy sequences, interferon induction suppression sequences or sequences having RNase suppression activity which are functionally expressed and are encoded within the intervening region (II). Thus, applicant was not possession of the claimed genus of constructs claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

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only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4 and 7 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Fire et al (USPN 6,506,559).

Fire et al (USPN 6,506,559) teach compositions for inhibiting the expression of a target gene, including compositions comprising antisense, ribozymes and siRNA. Fire teaches the introduction of siRNA into target cells for the inhibition of expression of a target gene, which siRNA construct is synthesized chemically or recombinantly from an appropriate expression vector, and is optionally expressed as two separate strands, or as a single strand with intervening sequences, and which chemically synthesized siRNA optionally comprises modifications for enhancing target binding, cellular uptake and stability, which self complementary strands of the siRNA optionally comprise a deleted, substituted or added nucleobase (see esp. col. 1-5; col. 7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 7-10, 18, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire (USPN 6,506,559) and Tuschl et al (WO 2001/75164), the combination further in view of Cabello et al (US 2004/0086911) and Satishchandran (US 2006/0084617).

The claims are drawn to compositions comprising a recombinant vector comprising self-complementary single strands comprising siRNA, which self complementary strands are components I and III, and an intervening sequence, II, optionally comprising between 7 to 12 nucleobases, or encoding a cytoplasm translocation sequence or an interferon induction suppressing sequence, and which recombinant vector further comprises a T7 or CMV promoter, and a termination sequence.

Fire et al (USPN 6,506,559) teach compositions for inhibiting the expression of a target gene, including compositions comprising antisense, ribozymes and siRNA. Fire teaches the introduction of siRNA into target cells for the inhibition of expression of a target gene, which siRNA construct is synthesized chemically or recombinantly from an appropriate expression vector, and is optionally expressed as two separate strands, or as a single strand with intervening sequences, and which chemically synthesized siRNA

optionally comprises modifications for enhancing target binding, cellular uptake and stability, which self complementary strands of the siRNA optionally comprise a deleted, substituted or added nucleobase (see esp. col. 1-5; col. 7).

Tuschl et al (WO 2001/75164) teach methods of manufacturing and using compositions comprising recombinant expression vectors encoding RNAi polynucleotides comprising three portions and having between 15-30 nucleotides, where two portions are self-complementary, comprising the target sequence of SEQ ID No. 1, and wherein some bases in portions I or III are deleted, substituted or added, which polynucleotide comprises DNA and RNA (page 4, lines 1-13; bridging paragraph, pages 4-5; page 7, lines 24-26; see example 5, fig. 14B, 16A-F; page 13, line 14-page 15, line 4; Accession No. AAS16113)

The primary references of Tuschl and Fire do not teach the intervening sequences between self-complementary strands comprising interferon induction suppressing sequences, nor the promoter driving expression of the siRNA construct comprising a T7 or CMV promoter sequence, and further comprising a termination sequence.

Cabello et al (US 2004/0086911) teach pharmaceutical compositions comprising recombinant expression constructs comprising CMV or T7 promoters for driving expression of the construct comprising siRNA for inhibiting expression of a target gene in a cell, and which expression vector also comprises a termination sequence. Cabello also teaches that siRNA induces the RNAi pathway, which in turn induces non-specific

reductions in gene expression which are triggered by activation of an interferon response (see pages 1-3 and 9, see esp. paragraphs 0008, 0140, 0151-0153).

Satishchandran (US 2006/0084617) teach compositions comprising recombinant expression constructs comprising inhibitory oligonucleotides for targeting genes involved in interferon responses (see pages 1; 3-5, 8; paragraphs 0201-0205).

It would have been obvious to one of ordinary skill in the art to design and chemically or recombinantly synthesize a nucleic acid construct comprising a continuous, single stranded molecule comprising siRNA from self complementary sequences and further comprising an intervening sequence allowing for a loop between the self complementary strands of the siRNA because Fire teaches recombinant constructs comprising these self complementary strands, optionally expressed as a single sequence. It would have been obvious to incorporate the well known T7 or CMV promoters in the recombinant construct, and a termination codon, because these promoters and in combination with a termination codon were well known in the art and used routinely to drive expression of recombinant constructs in target cells including mammalian target cells as taught previously by Cabello.

One of ordinary skill would have been motivated to include an inhibitory molecule which silences inteferon activation because siRNA was known in the art to generate interferon mediated, non-specific gene silencing effects in target cells and one would be motivated to control these non-specific effects so that one can better control the targeting and inhibition of desired target genes by designing the siRNA gene sequences to specifically target the target genes of interest, while inhibiting the unwanted, non-

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specific gene silencing reactions caused by interferon induction. Furthermore, both Satishchandran and Cabello taught the potential deleterious effects of interferon mediated responses in the immune system. One of ordinary skill in the art would have expected that the inclusion of interferon induction suppressing sequences would successfully diminish the unwanted side effects of interferon activated responses because Satishchandran taught the suppression of interferon activated responses using inhibitory oligonucleotides including antisense and siRNA, and placing the interferon induction suppressing sequences between the self complementary strands of the siRNA molecule would have been a matter of design choice.

For these reasons, the instant invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Douglas) Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
4-25-08

/Jane Zara/

Primary Examiner, Art Unit 1635